transfected cells, and recovering the desired protein from the medium. Besides urinary TBP-I, differentially spliced TBP-I can also be produced by this method.

It is noted that the examiner considers that the priority date for this application is July 12, 1990. While applicant continues to disagree with this conclusion, the point is presently moot as no intervening reference has been cited against any of the claims presently appearing in the case. Applicant explicitly does not concede the examiner's position and reserves the right to argue entitlement to an earlier priority date when and if any intervening reference is cited with respect to the present claims or with respect to any claim which is eventually prosecuted in this or any continuing application.

The examiner has objected to the disclosure because of a number of informalities. The examiner states that the pendency status of the related applications must be updated on page 1 of the specification and that sequence information is required, for example at page 8, lines 2 and 22, of the specification. This objection is respectfully traversed.

The pendency status of the related applications and indeed the identity of the related applications has now been updated on page 1 of the specification. Note that the declaration as filed indicated that the present application claimed benefit under 35 USC 120 of application no. 07/243,092. Accordingly, parent application 07/625,668 should be considered to have been a continuation-in-part of said application 07/243,092.

With respect to the required corrections concerning sequence information, it is respectfully pointed out that the quoted portion of 37 C.F.R. §1.821(d) does not require an insertion of a sequence identification number every time the specification refers to a figure of a drawing which includes a sequence. If the sequence were embedded in the text of the description, then a sequence identification number would have to be submitted thereafter. Every sequence discussed in the present specification appears in the sequence listing. The sequence identification numbers corresponding to the sequences presented in the drawing, appear in the description of the drawings at pages 4-7 of the present specification. It would exalt form over substance to interpret 37 C.F.R. §1.821(d) to require the insertion of a sequence identification number not only at page 8, lines 2 and 22, as indicated by the examiner, but also, if the examiner's logic is to be followed, at page 7, lines 11 and 14; page 8, line 8; page 11, line 8; page 13, lines 2, 5 and 6; page 14, lines 7, 14, 15, 19, 24 and 26; page 19, lines 2, 9, 25 and 26; page 20, lines 4, 17 and 18; page 21, lines 4, 15, 17 and 22; page 22, lines 1, 4, 7 and 11; etc. Indeed, by the examiner's logic, any time TBP-I is mentioned, a sequence identification number should be given. This is simply not required by the rules. One is permitted to refer to drawings and tables in the specification without reciting a specific sequence identification number as long as the description of the drawings and the table themselves set forth what the sequence identification numbers are.

Reconsideration and withdrawal of this part of the objection are therefore respectfully urged.

Claims 1-6 and 8-10 have been rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The examiner states that these claims recite a soluble protein having the characteristics of TBP-I, but it is not clear what applicants consider as being the characteristics of TBP-I. The examiner states that the specification does not disclose what the characteristics are or which specific features would be used to ascertain that the protein is TBP-I, and therefore the metes and bounds of the claims are unclear. The examiner further considers that claim 9 is indefinite because the specification discloses only the production of TBP-I by the CHO cells, while claim 9 depends on claim 8, which recites that the protein should not be TBP-I.

First of all, the rejection of claim 9 has now been obviated by the deletion of claim 9. With respect to the remaining claims, claim 1 has been amended to specify that the characteristics of TBP-I being referred to are the TNF binding characteristics. The specification discloses that this is the main characteristic of TBP-I in view of its name (TNF binding protein). See also page 3, lines 4-6, of the present specification. Thus, it is the ability of TBP-I to bind TNF which causes it to interfere with the binding of TNF to cells and thus to function as physiological inhibitors of TNF activity. As binding to TNF is a very easy characteristic to measure, this

recitation has now been added to the claim in order to obviate this part of the rejection. Reconsideration and withdrawal thereof is therefore respectfully urged.

Claims 1-6 and 8-10 have been rejected under 35 USC 112, first paragraph, because the specification, while enabling for making a soluble recombinant TBP-I protein by transfecting mammalian cells with a DNA encoding the whole human type-I TNF receptor, does not reasonably provide enablement for making any soluble TNF binding protein by transfecting any eukaryotic cells. The examiner states that the claim is too broad in view of the indefiniteness of the term "characteristics". Further, the examiner states that the term "eukaryotic cells" is too broad as one would not be able to predict whether the invention would work with non-mammalian cells. Further, the examiner states that the specification does not teach how one would produce "non-TBP-I" proteins. This rejection is respectfully traversed.

As indicated above, claim 1 has now been amended to specify that the characteristics of the protein being produced are the tumor necrosis factor binding characteristics of TBP-I. Furthermore, claim 1 has been amended to specify that the cells being transfected are mammalian cells. Furthermore, the examiner's comment about producing "non-TBP-I" protein indicates a possible misunderstanding of the present invention. The previously identified protein given the designation TBP-I was isolated from urine and contains an N-terminal amino acid sequence specified in U.S. application no. 07/243,092 (which has now been abandoned in favor of continuation application no. 07/876,828,

which has been allowed and will issue soon). However, the second paragraph on page 8 of the present specification indicates that the soluble proteins produced by the transfected cells according to the method of the present invention may have varying lengths, i.e., the N-terminus may begin anywhere between Ile(+1) and Asp(20) and may end between 180(Asn) and 182(Lys). Page 8, lines 12-14, state:

> All these soluble proteins, if biologically active with TBP-I like activity, are encompassed by the invention as precursors and analogs of TBP-I.

Thus, assuming there to be a specified TBP-I, i.e., that protein which was isolated from urine, any of the other sequences of varying lengths which are encompassed by the claim will be non-TBP-I proteins with the same biological activity as TBP-I. With this understanding, it is believed that the present specification is indeed fully enabling, particularly as claim 1 is presently amended. In any event, new claim 11 has now been added, specifying that the protein having the TNF binding characteristics of human TBP-I are those having the amino acid sequences set forth in claim 11, as supported by the portion of the specification discussed above. Accordingly, it is submitted that both claims 1 and 11 and all of the claims that depend therefrom are supported by an enabling disclosure. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 8 and 10 have been rejected under 35 USC 103(a) as being unpatentable over Loetscher or Schall in view of Livneh.

Claims 8 and 10 have now been deleted, thus obviating this rejection.

It is noted that the examiner has indicated that claims 1-6 are free of the prior art because Loetscher and Schall do not teach the invention of applicants which is claimed in claims 1-6. Applicant agrees with this indication by the examiner as to why these claims are free of the prior art and also for the reason that, if Loetscher and Schall had been references, they could have been overcome by establishing an earlier effective filing date or at least an earlier date of invention.

It is submitted that all the claims now present in the case clearly define over the references of record. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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